Enhanced generation of induced pluripotent stem cells from a subpopulation of human fibroblasts.

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Public Summary:
We observed that pluripotent stem cells, those that can make any cell type of the body, can be derived from a small subset of cells that are found in normal skin biopsies (skin cells). Previous studies suggested that the major reason for low efficiency in making reprogrammed pluripotent stem cell lines was that the genes used to induce pluripotency might not be highly expressed, the cell timing might be important and not often in the right part of the cycle, or that human cell reprogramming was stochastic with a random cause for low efficiency. This study suggests that it is a subset of cell types that is reprogrammed and thus, this small set of cells is efficiently reprogrammed while others are not reprogrammed at all or at very, very low levels. Results have implications for reprogramming of adult skin cells to pluripotent stem cells and for applications of those cells in regenerative medicine.

Scientific Abstract:
BACKGROUND: The derivation of induced pluripotent stem cells (iPSCs) provides new possibilities for basic research and novel cell-based therapies. Limitations, however, include our current lack of understanding regarding the underlying mechanisms and the inefficiency of reprogramming. METHODOLOGY/PRINCIPAL FINDINGS: Here, we report identification and isolation of a subpopulation of human dermal fibroblasts that express the pluripotency marker stage specific embryonic antigen 3 (SSEA3). Fibroblasts that expressed SSEA3 demonstrated an enhanced iPSC generation efficiency, while no iPSC derivation was obtained from the fibroblasts that did not express SSEA3. Transcriptional analysis revealed NANOG expression was significantly increased in the SSEA3 expressing fibroblasts, suggesting a possible mechanistic explanation for the differential reprogramming. CONCLUSIONS/SIGNIFICANCE: To our knowledge, this study is the first to identify a pluripotency marker in a heterogeneous population of human dermal fibroblasts, to isolate a subpopulation of cells that have a significantly increased propensity to reprogram to pluripotency and to identify a possible mechanism to explain this differential reprogramming. This discovery provides a method to significantly increase the efficiency of reprogramming, enhancing the feasibility of the potential applications based on this technology, and a tool for basic research studies to understand the underlying reprogramming mechanisms.